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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket No: VOS-42 CON

In re patent application of

BRINKMANN, ULRICH et al.

Serial No. 10/627,253

Filed: July 24, 2003

For: POLYMORPHISMS IN THE HUMAN GENE FOR THE MULTIDRUG  
RESISTANCE-ASSOCIATED PROTEIN 1 (MRP-1) AND THEIR USE IN  
DIAGNOSTIC AND THERAPEUTIC APPLICATIONS

STATEMENT TO SUPPORT FILING AND SUBMISSION IN  
ACCORDANCE WITH 37 C.F.R. §§ 1.821-1.825

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
Mail Stop SEQUENCE

Sir:

In connection with a Sequence Listing submitted concurrently  
herewith, the undersigned hereby states that:

1. the submission, filed herewith in accordance with 37  
C.F.R. § 1.821(g), does not include new matter;
2. the content of the attached paper copy and the  
attached computer readable copy of the Sequence Listing, submitted in  
accordance with 37 C.F.R. § 1.821(c) and (e), respectively, are the same.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "David M. Narkunas".

David M. Narkunas  
Reg. No. 53,370

March 25, 2004

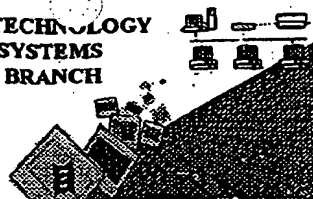
Date

HARBOR CONSULTING IP SERVICES, INC.  
1500A Lafayette Road, #262  
Portsmouth, N.H.  
800-318-3021

## **RAW SEQUENCE LISTING ERROR REPORT**



BIOTECHNOLOGY  
SYSTEMS  
BRANCH



The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 10/627,253  
Source: IFWO  
Date Processed by STIC: 1/4/04

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221

Effective 12/13/03: TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE CHECKER  
VERSION 4.1 PROGRAM, ACCESSIBLE THROUGH THE U.S. PATENT AND  
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

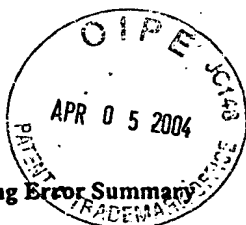
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry directly to (EFFECTIVE 12/01/03):  
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 4B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03

# Raw Sequence Listing Error Summary



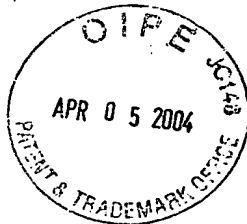
SERIAL NUMBER: 10/627,253

## ERROR DETECTED

## SUGGESTED CORRECTION

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

- 1 ☐ **Wrapped Nucleics**  
**Wrapped Aminos** The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."
- 2 ☐ **Invalid Line Length** The rules require that a line not exceed 72 characters in length. This includes white spaces.
- 3 ☐ **Misaligned Amino Numbering** The numbering under each 5<sup>th</sup> amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.
- 4 ☒ **Non-ASCII** The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.
- 5 ☒ **Variable Length** Sequence(s) 371-372 contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.
- 6 ☐ **PatentIn 2.0 "bug"** A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) \_\_\_\_\_. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.
- 7 ☐ **Skipped Sequences (OLD RULES)** Sequence(s) \_\_\_\_\_ missing. If intentional, please insert the following lines for each skipped sequence:  
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)  
This sequence is intentionally skipped  
  
Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.
- 8 ☐ **Skipped Sequences (NEW RULES)** Sequence(s) \_\_\_\_\_ missing. If intentional, please insert the following lines for each skipped sequence.  
<210> sequence id number  
<400> sequence id number  
000
- 9 ☐ **Use of n's or Xaa's (NEW RULES)** Use of n's and/or Xaa's have been detected in the Sequence Listing.  
Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.  
In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.
- 10 ☐ **Invalid <213> Response** Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence
- 11 ☐ **Use of <220>** Sequence(s) \_\_\_\_\_ missing the <220> "Feature" and associated numeric identifiers and responses.  
Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.  
(See "Federal Register," 0001/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)
- 12 ☐ **PatentIn 2.0 "bug"** Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.
- 13 ☐ **Misuse of n/Xaa** "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid



IFWO

## RAW SEQUENCE LISTING

PATENT APPLICATION: US/10/627,253

DATE: 01/04/2004

TIME: 10:35:10

Input Set : A:\PTO.FG.txt

Output Set: N:\CRF4\01042004\J627253.raw

3 <110> APPLICANT: Ulrich Brinkmann  
4 Sven Hoffmeyer  
5 Esther Mornhinweg  
7 <120> TITLE OF INVENTION: Polymorphisms in the human gene for the multidrug  
assistance-associated  
8 protein 1 (MRP-1) and their use in diagnostic and therapeutic applications  
10 <130> FILE REFERENCE: VOS-42 CON  
12 <140> CURRENT APPLICATION NUMBER: US 10/627,253  
--> 13 <141> CURRENT FILING DATE: 2003-07-24  
15 <150> PRIOR APPLICATION NUMBER: WO 02/059142 A2  
16 <151> PRIOR FILING DATE: 2002-01-25  
17 <150> PRIOR APPLICATION NUMBER: EP 01 10 1651.6  
18 <151> PRIOR FILING DATE: 2001-01-26  
20 <160> NUMBER OF SEQ ID NOS: 405  
22 <170> SOFTWARE: PatentIn Ver. 2.1

## ERRORED SEQUENCES

Does Not Comply  
Corrected Diskette Needed

pp1-2,4

5611 <210> SEQ ID NO: 371  
5612 <211> LENGTH: (52) SI shown  
5613 <212> TYPE: DNA  
5614 <213> ORGANISM: Artificial DNA Sequence  
5616 <220> FEATURE:  
5617 <221> NAME/KEY: source  
5619 <223> OTHER INFORMATION: /note="Description of Artificial DNA Sequence: sequence of  
able 3"  
5621 <220> FEATURE:  
5622 <223> OTHER INFORMATION: n = gcc gcc gcc or deleted OK  
5624 <400> SEQUENCE: 371  
--> 5625 tccctgcgcc gcgcgcgcgc ccgcgcgcgc cgcgcgcgc nagoctag cg  
5628 <210> SEQ ID NO: 372  
5629 <211> LENGTH: (52) SI  
5630 <212> TYPE: DNA  
5631 <213> ORGANISM: Artificial DNA Sequence  
5633 <220> FEATURE:  
5634 <221> NAME/KEY: source  
5636 <223> OTHER INFORMATION: /note="Description of Artificial DNA Sequence: sequence of  
able 3"  
5638 <220> FEATURE:  
5639 <223> OTHER INFORMATION: n = ggc ggc ggc or deleted  
5641 <400> SEQUENCE: 372  
--> 5642 cgctagcgcct nggcgcgcgc ggcgcgcgcgc gcgcgcgcgc cgcgcgcgc ga

(52) SI

(52) SI

PSI: all bases MUST be in lower-case letters

le://C:\CRF4\Outhold\VsJ627253.htm

see p.2 for more errors

1/4/04

10/627,253

2

<400> 405  
ccccccgccc gggcg

15

??

??

(...Continued)

(Continued...)

112

*delete at end of file*

RAW SEQUENCE LISTING ERROR SUMMARY  
PATENT APPLICATION: US/10/627,253

DATE: 01/04/2004  
TIME: 10:35:12

Input Set : A:\PTO.FG.txt  
Output Set: N:\CRF4\01042004\J627253.raw

Invalid Line Length:

These rules require that a line not exceed 72 characters in length. This includes spaces.

eq#:323; Line(s) 4858  
eq#:325; Line(s) 4896  
eq#:327; Line(s) 4934  
eq#:328; Line(s) 4955  
eq#:363; Line(s) 5501  
eq#:364; Line(s) 5518  
eq#:367; Line(s) 5563  
eq#:368; Line(s) 5580  
eq#:371; Line(s) 5625  
eq#:372; Line(s) 5642  
eq#:375; Line(s) 5687  
eq#:376; Line(s) 5704  
eq#:379; Line(s) 5749  
eq#:380; Line(s) 5766

4

VARIABLE LOCATION SUMMARY  
PATENT APPLICATION: US/10/627,253

DATE: 01/04/2004  
TIME: 10:35:12

Input Set : A:\PTO.FG.txt  
Output Set: N:\CRF4\01042004\J627253.raw

Presence of n's or Xaa's (NEW RULES):

Presence of n's and/or Xaa's have been detected in the Sequence Listing.  
Presence of <220> to <223> is MANDATORY if n's or Xaa's are present.  
In <220> to <223> section, please explain location of n or Xaa, and which  
residue n or Xaa represents.

Seq#:85; N Pos. 11  
Seq#:86; N Pos. 11  
Seq#:97; N Pos. 11  
Seq#:98; N Pos. 11  
Seq#:103; N Pos. 11  
Seq#:104; N Pos. 11  
Seq#:229; N Pos. 11  
Seq#:230; N Pos. 11  
Seq#:241; N Pos. 11  
Seq#:242; N Pos. 11  
Seq#:265; N Pos. 11  
Seq#:266; N Pos. 11  
Seq#:359; N Pos. 11  
Seq#:360; N Pos. 11  
Seq#:363; N Pos. 47  
Seq#:364; N Pos. 11  
Seq#:367; N Pos. 44  
Seq#:368; N Pos. 11  
Seq#:371; N Pos. 41  
Seq#:372; N Pos. 11  
Seq#:375; N Pos. 38  
Seq#:376; N Pos. 11  
Seq#:379; N Pos. 29  
Seq#:380; N Pos. 11  
Seq#:383; N Pos. 11  
Seq#:384; N Pos. 11  
Seq#:395; N Pos. 11  
Seq#:396; N Pos. 11  
Seq#:402; Xaa Pos. 6  
Seq#:404; Xaa Pos. 6



VERIFICATION SUMMARY  
PATENT APPLICATION: US/10/627,253

DATE: 01/04/2004  
TIME: 10:35:12

Input Set : A:\PTO.FG.txt  
Output Set: N:\CRF4\01042004\J627253.raw

:13 M:271 C: Current Filing Date differs, Replaced Current Filing Date  
:1299 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:85  
:1299 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:85 after pos.:0  
:1316 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:86  
:1316 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:86 after pos.:0  
:1479 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:97  
:1479 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:97 after pos.:0  
:1496 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:98  
:1496 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:98 after pos.:0  
:1568 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:103  
:1568 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:103 after pos.:0  
:1585 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:104  
:1585 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:104 after pos.:0  
:3451 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:229  
:3451 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:229 after pos.:0  
:3468 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:230  
:3468 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:230 after pos.:0  
:3631 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:241  
:3631 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:241 after pos.:0  
:3648 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:242  
:3648 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:242 after pos.:0  
:3991 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:265  
:3991 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:265 after pos.:0  
:4008 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:266  
:4008 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:266 after pos.:0  
:5439 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:359  
:5439 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:359 after pos.:0  
:5456 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:360  
:5456 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:360 after pos.:0  
:5501 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:363  
:5501 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:363 after pos.:0  
:5501 M:112 C: (48) String data converted to lower case,  
:5518 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:364  
:5518 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:364 after pos.:0  
:5518 M:112 C: (48) String data converted to lower case,  
:5563 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:367  
:5563 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:367 after pos.:0  
:5563 M:112 C: (48) String data converted to lower case,  
:5580 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:368  
:5580 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:368 after pos.:0  
:5580 M:112 C: (48) String data converted to lower case,  
:5625 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:371  
:5625 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:371 after pos.:0  
:5625 M:254 E: No. of Bases conflict, LENGTH:Input:52 Counted:51 SEQ:371 ✓  
:5625 M:112 C: (48) String data converted to lower case,  
:5625 M:252 E: No. of Seq. differs, <211> LENGTH:Input:52 Found:51 SEQ:371  
:5642 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:372  
:5642 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:372 after pos.:0

VERIFICATION SUMMARY

PATENT APPLICATION: US/10/627,253

DATE: 01/04/2004

TIME: 10:35:12

Input Set : A:\PTO.FG.txt

Output Set: N:\CRF4\01042004\J627253.raw

:5642 M:254 E: No. of Bases conflict, LENGTH:Input:52 Counted:51 SEQ:372  
:5642 M:112 C: (48) String data converted to lower case,  
:5642 M:252 E: No. of Seq. differs, <211> LENGTH:Input:52 Found:51 SEQ:372  
:5687 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:375  
:5687 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:375 after pos.:0  
:5687 M:112 C: (48) String data converted to lower case,  
:5704 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:376  
:5704 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:376 after pos.:0  
:5704 M:112 C: (48) String data converted to lower case,  
:5749 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:379  
:5749 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:379 after pos.:0  
:5749 M:112 C: (48) String data converted to lower case,  
:5766 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:380  
:5766 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:380 after pos.:0  
:5766 M:112 C: (48) String data converted to lower case,  
:5811 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:383  
:5811 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:383 after pos.:0  
:5828 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:384  
:5828 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:384 after pos.:0  
:5998 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:395  
:5998 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:395 after pos.:0  
:6015 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:396  
:6015 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:396 after pos.:0  
:6109 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:402  
:6109 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:402 after pos.:0  
:6142 M:258 W: Mandatory Feature missing, <222> Tag not found for SEQ ID#:404  
:6142 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:404 after pos.:0  
:6164 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1  
:6166 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:405  
:6166 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1  
:6167 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:405  
:6167 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1  
:6169 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:405  
:6169 M:334 W: (2) Invalid Amino Acid in Coding Region, NUMBER OF INVALID KEYS:1  
:6178 M:336 W: Invalid Amino Acid Number in Coding Region, SEQ ID:405